MedicalXpress

Gene responsible for relapses in young leukemia patients

October 26 2011

One of the causes of resistance to cancer treatment in children is now beginning to be elucidated. Acute lymphoblastic leukemia patients with a particular form of the ATF5 gene are at higher risk of having a relapse when treated with *E. coli* asparaginase, a key chemotherapy drug for this type of leukemia. This is what a study by Dr. Maja Krajinovic published in the Blood, the journal of the American Society of Hematology, reveals Dr. Krajinovic is an investigator at the Sainte-Justine University Hospital Research Center, which is affiliated with the University of Montreal.

Dr. Krajinovic's team focused on asparaginase, one of the drugs in a chemotherapy "cocktail" administered to young patients during the intensification phase of their treatment.

They observed that *E. coli* asparaginase therapy was associated with an increase in relapses when administered to patients who had particular polymorphism (special form) of the ATF5 gene. In fact, this gene regulates asparagine synthetase, an enzyme that produces asparagine, which in turn feeds cancer cells.

"In the presence of this polymorphism that, as we demonstrated, modifies the transcription rate of the ATF5 gene, it is possible that the medication, rather than preventing the proliferation of leukemia cells by reducing the rate of asparagine, does just the opposite by creating feedback that triggers cancer cells to produce asparagine themselves," explains Dr. Krajinovic.

The discovery of a form of gene associated with high rates of relapse during treatment with E.coli asparaginase opens the door to the possibility of selecting a type of pharmacological treatment based on a patient's genetic profile, an approach that reflects the shift toward personalized medicine. "If a DNA test detects the implicated polymorphisms in children, it will be possible to predict the risk of relapse or side effects," exclaimed Dr. Krajinovic. "The clinician can then propose an alternative treatment or adjust the dose accordingly."

Since the introduction of combination chemotherapy, the rate of pediatric survival without relapse has skyrocketed to about 80%. Yet some patients still resist treatment or present side effects. Pharmacogenetic research strategies involve studying the reaction to each drug used for combined chemotherapy based on various patient genetic profiles so as to design treatment plans that increase efficacy and reduce side effects in patients. Dr. Krajinovic has published a number of similar studies that focus on antifolate, another drug used in combination regimens to treat acute lymphoblastic leukemia.

Provided by University of Montreal